

Appln No. 10/561.631
Amdt date June 16, 2010
Reply to Office action of March 3, 2010

Amendments to the Drawings

The attached sheets of drawings include changes to FIGS. 1 and 2. These sheets, which include FIGS. 1 and 2, replace the original sheets including FIGS. 1 and 2.

Attachment: Replacement Sheets for FIGS. 1 and 2.

REMARKS/ARGUMENTS

Claims 1-15 are pending in the above-referenced application. Claims 1 and 8-11 have been withdrawn from consideration.

Claims 1 and 2 have been amended to further define the Applicant's invention. Claim 4 has been amended to be consistent with the specification. Dependent claims 5-7 have been amended to remove dependency from multiple dependent claims. New claims 12-15 have been added. Support for the amendment can be found in the instant specification, among other places, on page 6, lines 23-24; page 7, lines 7-20, page 8, lines 21-23; page 9, lines 1-6 and lines 13-14; and page 10, lines 13-20. No new matter has been added.

This is a response to the non-final Office Action dated March 3, 2010 wherein the Examiner objected to: (1) the drawings for not being in compliance with PCT Rule 11; (2) the specification as failing to provide proper antecedent basis for the claimed subject matter; and (3) claims 5-7 under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claims.

The Examiner further rejected: (1) claims 2 and 3 under 35 U.S.C. 102(b) as being anticipated by PCT Publication No. WO 94/22426 (Heckenmüller); (2) claim 2 under 35 U.S.C. 102(b) as being anticipated by Trotter ("Effects of Postnatal Estradiol and Progesterone Replacement in Extremely Preterm Infants"); (3) claim 4 under 35 U.S.C. 103(a) as being unpatentable over Heckenmüller; and (4) claims 3 and 4 under 35 U.S.C. 103(a) as being unpatentable over Trotter.

Applicant respectfully thanks the Examiner for the time and effort in preparing and issuing the instant Action.

In view of the amended claims and the remarks that follow, reconsideration of the rejections and a notice of allowance are respectfully solicited.

ELECTION/RESTRICTIONS

The Examiner has required election in the present application between:

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Group I, claim 1, drawn to a process for the preparation of isotonic oil emulsions containing estrogen and progestagen;

Group II, claims 2-7, drawn to a hormone-containing isotonic oil emulsion;

Group III, claim 8, drawn to the use of the isotonic oil emulsion for preparing a medicament for postnatal hormone substitution in premature babies;

Group IV, claim 9, drawn to the use of the isotonic oil emulsion for preparing a medicament for the treatment of neurological damage after stroke; and

Group V, claim 11, drawn to a process for the treatment of neurological damage after strokes by using the isotonic emulsion.

Election:

During a telephone conversation with the Examiner on January 20, 2010, Applicant provisionally elected claims 2-7 with traverse. Applicant hereby affirms election of claims 2-7 for the purpose of examination of the present application. Applicant notes that claim 1, which is drawn to a process for making the products recited in elected claims 2 to 7, will be rejoined once the product claims are found allowable as per MPEP § 806.05(f).

Objection to the drawings

The Examiner objected to the drawings for failing to comply with PCT Rule 11. The drawings have been amended to comply with PCT Rule 11.13(a) and 11.13(e). Specifically, the lettering in the Figures has been changed to English and the drawings have been corrected to contain well-defined lines. In view of the enclosed amended drawings, rescission of the objection to the drawings is respectfully solicited.

Objection to the Specification

The Examiner objected to the specification for failing to provide proper antecedent basis for the claimed subject matter as recited in claim 4. Claim 4 has been amended as indicated above to be consistent with the specification. In view of the amendment, rescission of the objection is respectfully solicited.

Claim Objections

The Examiner objected to claims 5-7 under 37 CFR 1.75(c) for being dependent from multiple dependent claims. Claims 5-7 have been amended as indicated above to remove the informalities. In view of the amendment, rescission of the claim objections is respectfully solicited.

§ 102(b) Rejection of Claims 2 and 3 over Heckenmüller et al.

Claims 2 and 3 are rejected under 35 U.S.C § 102(b) as being anticipated by Heckenmüller et al.

In rejecting the foregoing claims, the Examiner takes the position that the cited reference teaches all the elements of the pending claims either explicitly or inherently.

Preliminarily, for a reference to anticipate a claimed invention under §102(b), it must adequately meet the terms of the claimed invention interpreted in light of the specification of the application. As set forth in the statute, the single prior art reference must disclose each and every element of the claim under consideration. Moreover, it cannot be rebuilt or reoriented by the utilization of Applicant's teachings in an attempt to create an anticipatory structure.

Amended Claim 2 recites:

2. (Currently Amended) A hormone-containing isotonic oil emulsion for intravenous administration comprising:
 - at least one of progestagens and estrogens;
 - an oil phase;
 - an antioxidant;
 - an emulsifier; and
 - an aqueous phase;wherein the at least one of progestagens and estrogens are dissolved in the oil phase prior to being mixed with the aqueous phase.

Thus, amended claim 2 is directed to an oil emulsion for intravenous administration comprising, among other things, at least one of the hormones of progestagens and estrogens, an oil phase; an antioxidant; an emulsifier and an aqueous phase. Claim 2 further specifies that the at least one of progestagens and estrogens are dissolved in the oil phase prior to being mixed with the aqueous phase.

In contrast, the '426 Heckenmüller publication is directed to a composition suitable for the transmucosal (e. g. nasal route) administration of the natural human sex hormones 17- β -estradiol or progesterone (page 4, lines 11-14). Heckenmüller teaches that these natural sex hormones have very limited oral effectiveness, and intravenous or intramuscular administration of the sex hormones is inconvenient and carries a potential risk for infections (page 1, line 38 to page 2, line 10). Thus, Heckenmüller teaches away from administering the natural sex hormones intravenously. A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. *In re Gurley*, 27 F. 3d 551, 553 (Fed. Cir. 1994).

Heckenmüller teaches dissolving the hormones 17- β -estradiol and/or progesterone in an oil phase before mixing it with the water phase (page 5, lines 21-24). The oil phase is an artificial or natural oil or mixture thereof (page 6, line 5). Heckenmüller's formulation also contains lecithin from egg or soybean predissolved in an oily liquid (page 6, lines 1-14). Optionally, non-ionic emulsifiers, including Tween, Puluronic F58 etc., and preservatives, including benzalkonium chloride or sorbitol, sodium edentate, are added. As described, Heckenmüller's composition does not comprise any antioxidant.

Antioxidants, as understood by a skilled artisan, are used for protection from reactive oxygen species such as hydrogen peroxide (H_2O_2), hypochlorous acid (HOCl), and free radicals such as the hydroxyl radical ($\cdot OH$) and the superoxide anion ($O_2^{\cdot -}$). These radicals are particularly unstable and can damage cells by starting chemical chain reactions such as lipid peroxidation, or by oxidizing DNA or proteins. Damage to DNA can cause mutations and possibly cancer, while damage to proteins causes enzyme inhibition, denaturation and protein degradation¹. Thus, antioxidants are important for an oil emulsion for intravenous administration since the oil emulsion comes into contact with internal organs and tissues. As Heckenmüller's composition is directed to a nasal formulation, to be applied outside the body, and furthermore,

¹ <http://en.wikipedia.org/wiki/Antioxidant>

as set forth above, teaches away from intravenous administration, therefore a skilled artisan would not have been motivated to add antioxidants to Heckenmüller's nasal spray.

Thus, Applicant respectfully submits that the '426 Heckenmüller publication fails to anticipate claim 2 under § 102(b), since it fails to disclose each and every element of the claim under consideration. Since claims 3 and 5-7 depend from claim 2, they too are allowable for at least the same reason.

§ 102(b) Rejection of Claim 2 over Trotter et al.

Claim 2 is rejected under 35 U.S.C § 102(b) as being anticipated by Trotter et al.

Trotter et al. describe a hormone replacement solution for use in extremely preterm infants (Abstract). According to Trotter, 17- β -estradiol and progesterone are diluted in 98% ethanol and added to a phospholipid-stabilized soybean oil emulsion such as Intralipid (Pharmacia & Upjohn, Inc.) for parenteral administration (page 4532, first column, last paragraph). Intralipid² from Pharmacia & Upjohn contains purified soybean oil, purified egg phospholipids, glycerol in water. As described, the hormones 17- β -estradiol and progesterone are diluted in 98% ethanol before being added to Intralipid. Furthermore, as described, Trotter's hormone replacement solution does not contain any antioxidant. Therefore, Trotter does not disclose an oil emulsion comprising at least one of progestagens and estrogens, an oil phase, an antioxidant and an aqueous phase wherein the at least one of progestagens and estrogens are dissolved in the oil phase prior to being mixed with the aqueous phase, as recited in part in claim 2.

Thus, Applicant respectfully submits that the Trotter publication fails to anticipate the claim 2 under § 102(b), since it fails to disclose each and every element of the pending claim. Since claims 5-7 depend from claim 2, they too are allowable over the cited reference for at least the same reason.

§ 103(a) Rejection of Claim 4 by Heckenmüller

² [http://www.rxmed.com/b.main/b2.pharmaceutical/b2.1.monographs/CPS-%20Monographs/CPS-%20\(General%20Monographs-%20I\)/INTRALIPID.html](http://www.rxmed.com/b.main/b2.pharmaceutical/b2.1.monographs/CPS-%20Monographs/CPS-%20(General%20Monographs-%20I)/INTRALIPID.html)

Claim 4 is rejected as unpatentable under § 103(a) over Heckenmüller.

In rejecting claim 4, the Examiner conceded that Heckenmüller does not teach the weight percent specified in claim 4. The Examiner that “it would have been obvious to a person having ordinary skill in the art at the time the invention is made to employ said amounts, thus arriving at the claimed invention” (Office Action, page 9).

Claim 4 depends from claim 2. As set forth above, Heckenmüller fails to anticipate claim 2 for not disclosing each and every element of the pending claim. As the Examiner merely relies on the knowledge of a skilled artisan to “manipulate the amounts of the hormones . . . by routine experimentation” (Office Action, page 9), a position that Applicant does not concede to, Heckenmüller in view of a person of ordinary skill in the art still fails to disclose or suggest all the elements and limitations of claim 2. Thus, Heckenmüller fails to render claim 2 obvious under § 103(a). Claim 4 depends from claim 2 and therefore is also allowable for at least the same reason.

§ 103(a) Rejection of Claims 3 and 4 by Trotter et al.

Claims 3 and 4 are rejected as unpatentable under § 103(a) over Trotter.

In rejecting claim 3 and 4, the Examiner conceded that Trotter does not teach the progesterone:estrogen ratio recited in claim 3 or the weight amounts specified in claim 4. The Examiner concluded that it would have been obvious to a person having ordinary skill in the art at the time the invention is made to manipulate the ratios or the amounts of the hormones by routine experimentation to arrive at the claimed invention. (Office Action, page 10).

Claims 3 and 4 depend from claim 2. As set forth above, Trotter fails to anticipate claim 2 for not disclosing each and every element of the pending claim. As the Examiner merely relied on the knowledge of a skilled artisan to manipulate the amounts of the ratios or the amounts of hormones by routine experimentation, a position that Applicant does not concede to, Applicant respectfully submits that Trotter in view of a person of ordinary skill in the art still fails to disclose or suggest all the elements of claim 2. Thus, Trotter fails to render claim 2 obvious

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under § 103(a). Claims 3 and 4 depend from claim 2 and therefore are also allowable for at least the same reason.

New claims 12-15

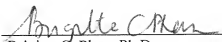
Newly added claims 12-15 depend either directly or indirectly from claim 2. As set forth above, both of the cited references fail to anticipate independent claim 2 under § 102(b) for not disclosing each and every element of the pending claim. Thus, claims 12-15 are also allowable over the cited references for at least the same reason.

CONCLUSION

In view of the foregoing arguments, Applicant respectfully submits that claims 2-7 and 12-15 are patentable and allowance is respectfully solicited.

Should the Examiner wish to speak with Applicant's attorney, she is invited to contact the undersigned at the telephone number identified below.

Respectfully submitted,
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